

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
In The Name Of ALLAH
The Most Gracious, The Most Merciful





Armed Forces College of Medicine AFCM



Drugs used to treat bronchial asthma and COPD (1)

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Khorshid***



INTENDED LEARNING OBJECTIVES (ILO)



By the end of this lecture the student will be able to:

1. Classify the drugs used in treatment of bronchial asthma
2. Classify the short term relievers of bronchial asthma (bronchodilators).
3. Explain the mechanism of action and adverse effects of the bronchodilators.



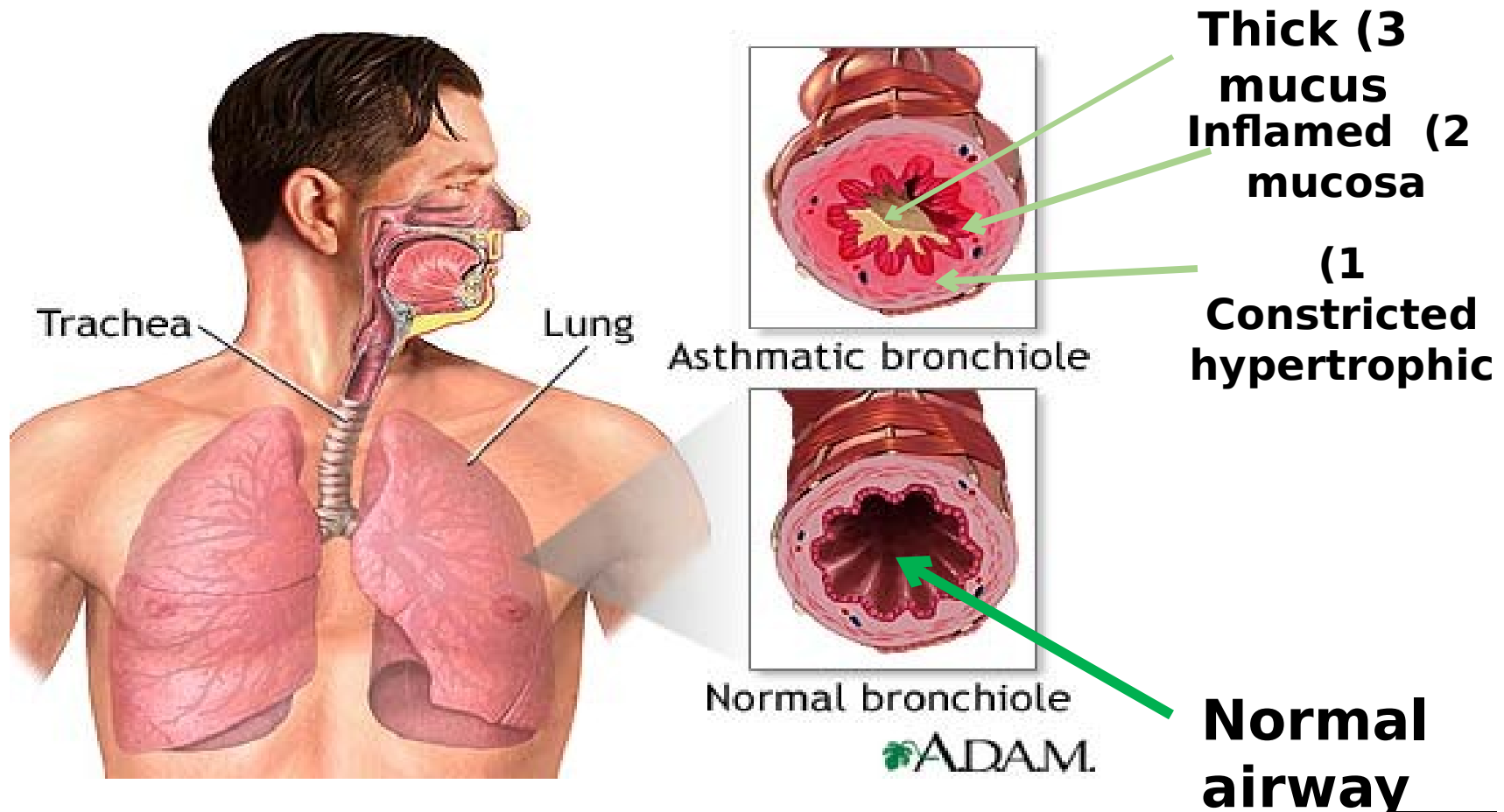
Bronchial Asthma

Clinically:

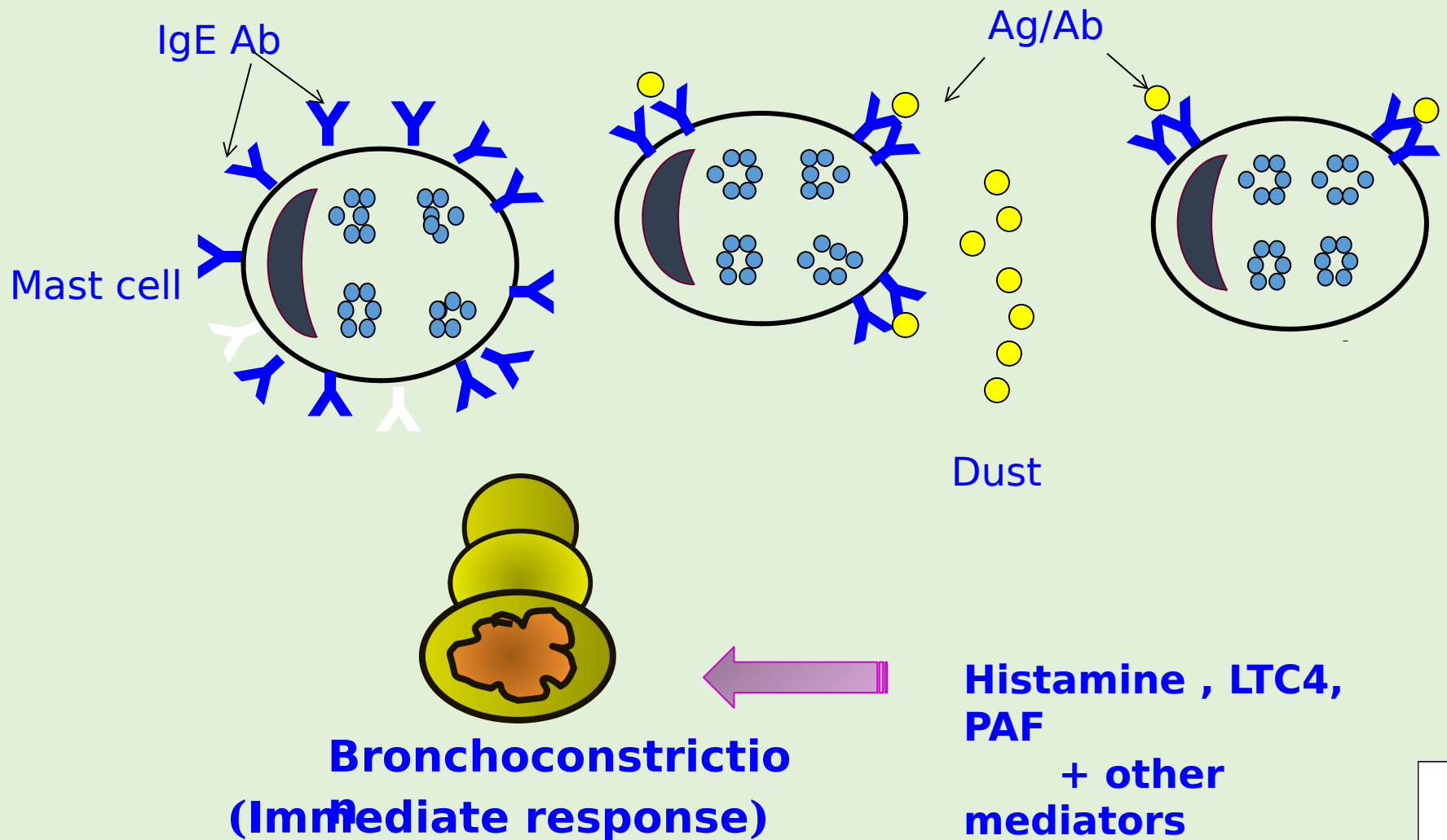
**recurrent bouts of coughing,
shortness
of breath and wheezing.**



: During an attack



Pathogenesis of asthma



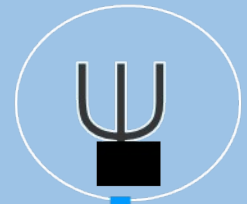
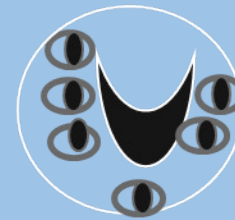
Pathogenesis of asthma

**Histamine , LTC4,
PAF
+ other
mediators**

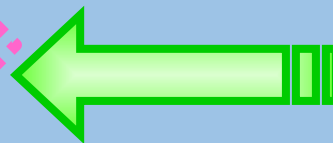


Eosinophil

Neutrophil



**Allergic & inflammatory
mediators**

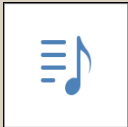


**Edema, mucus
,hypersecretion
smooth muscle
&contraction**

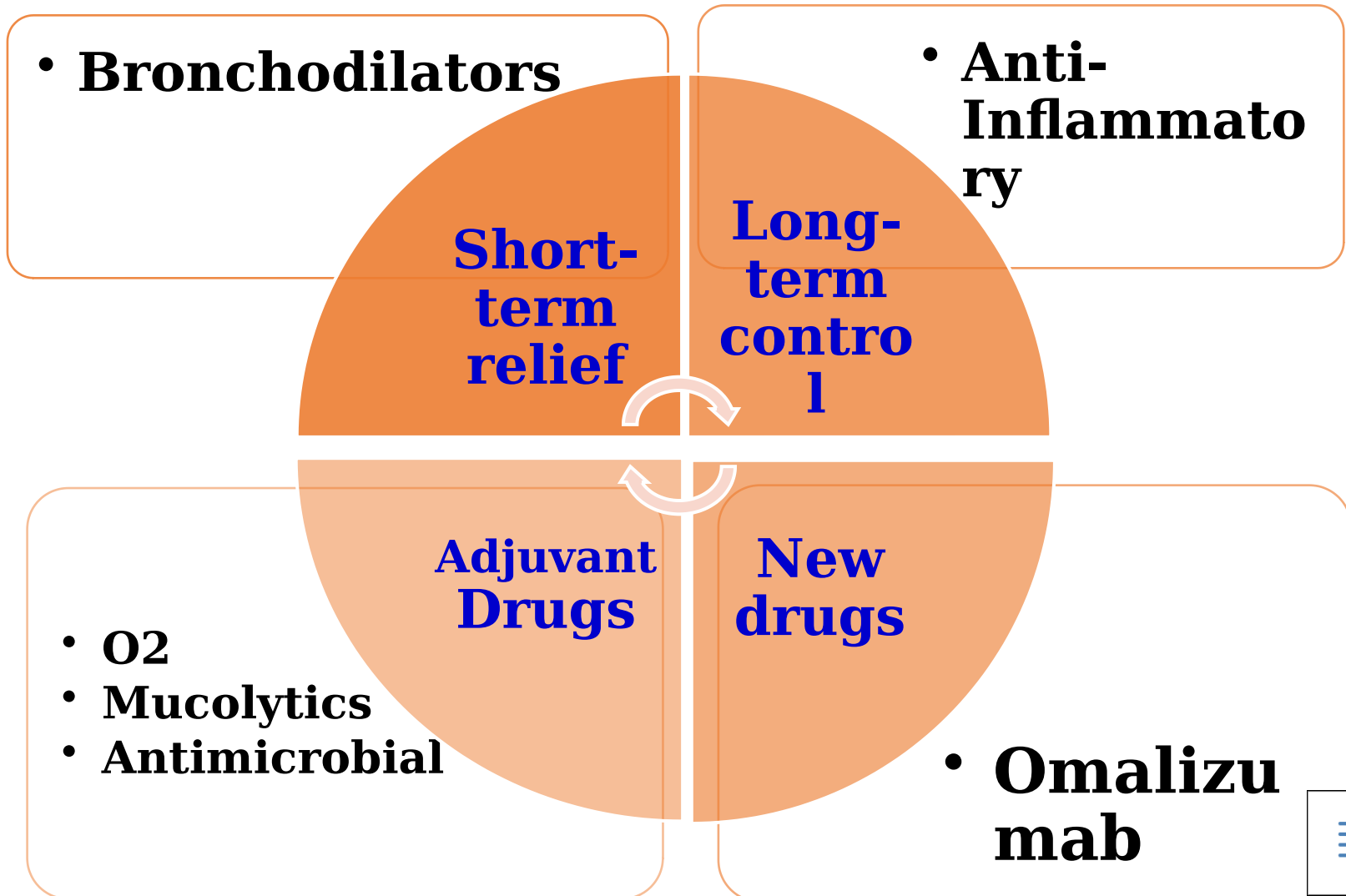
**bronchial reactivity
Late
response**



CLASSIFICATION	BRONCHO-CONSTRICTIVE EPISODES	RESULTS OF PEAK FLOW OR SPIROMETRY
Intermittent	Less than 2 days per week	Near normal*
Mild persistent	More than 2 days per week, not daily	Near normal*
Moderate persistent	Daily	60% to 80% of normal
Severe persistent	Continual	Less than 60% of normal



ing Treatment of Bronchial Asthma



Short- term relief

Bronchodilators

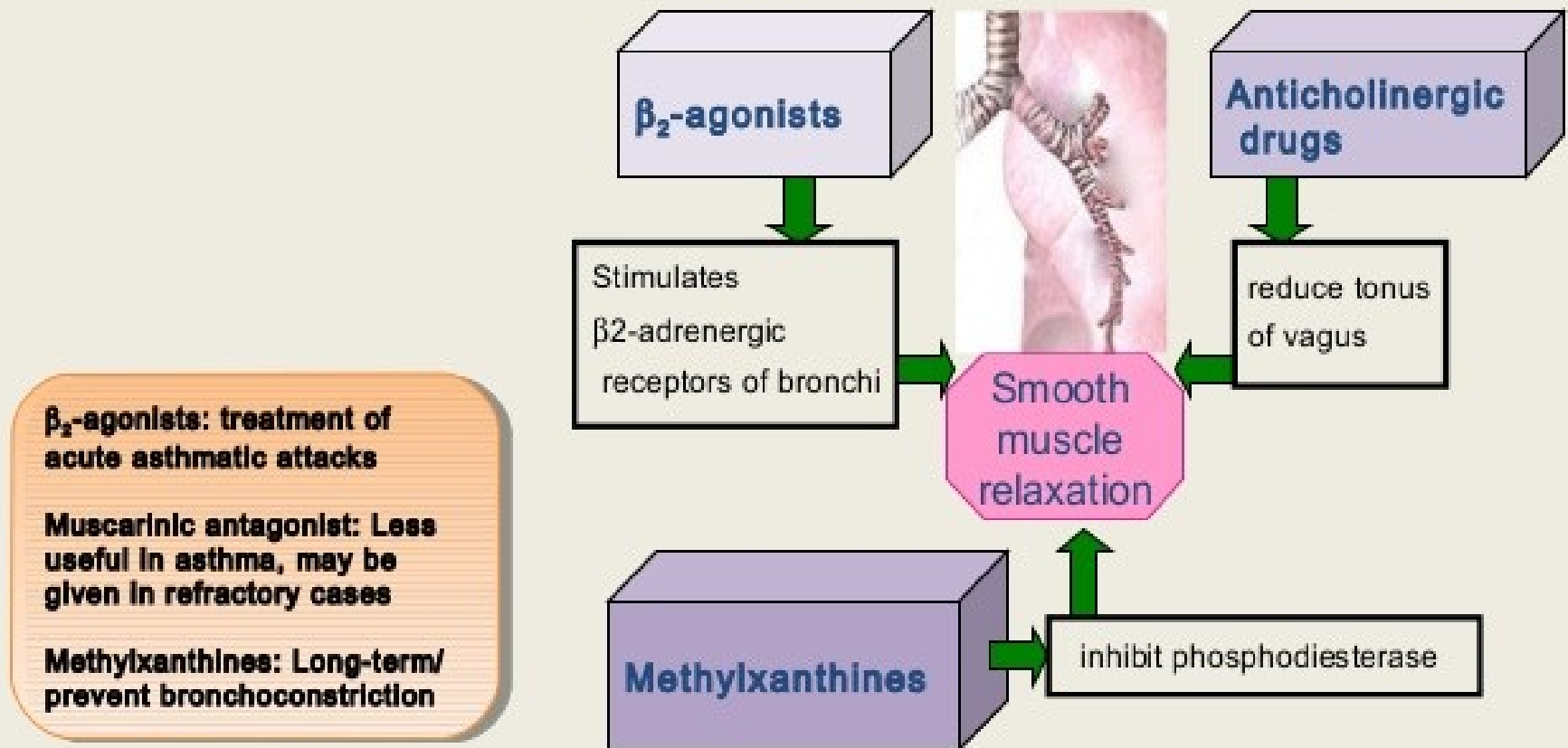
Sympathomimetics (β -Agonists) (1

**Parasympatholytics (Anti- (2
muscarinic)**

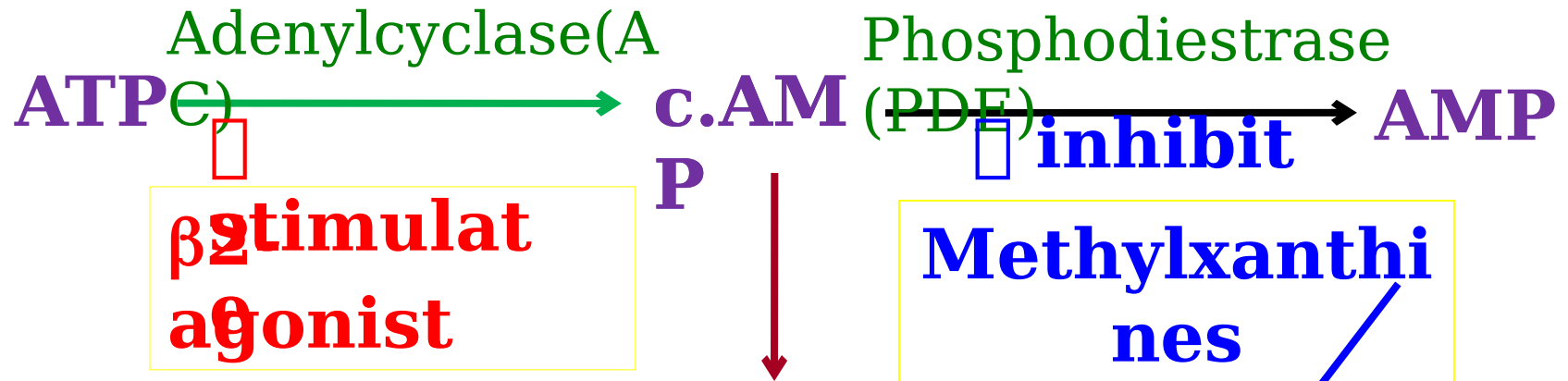
.Methyl-xanthines (3



Bronchodilators



Bronchodilators



Muscarinic antagonist

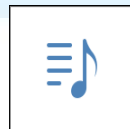
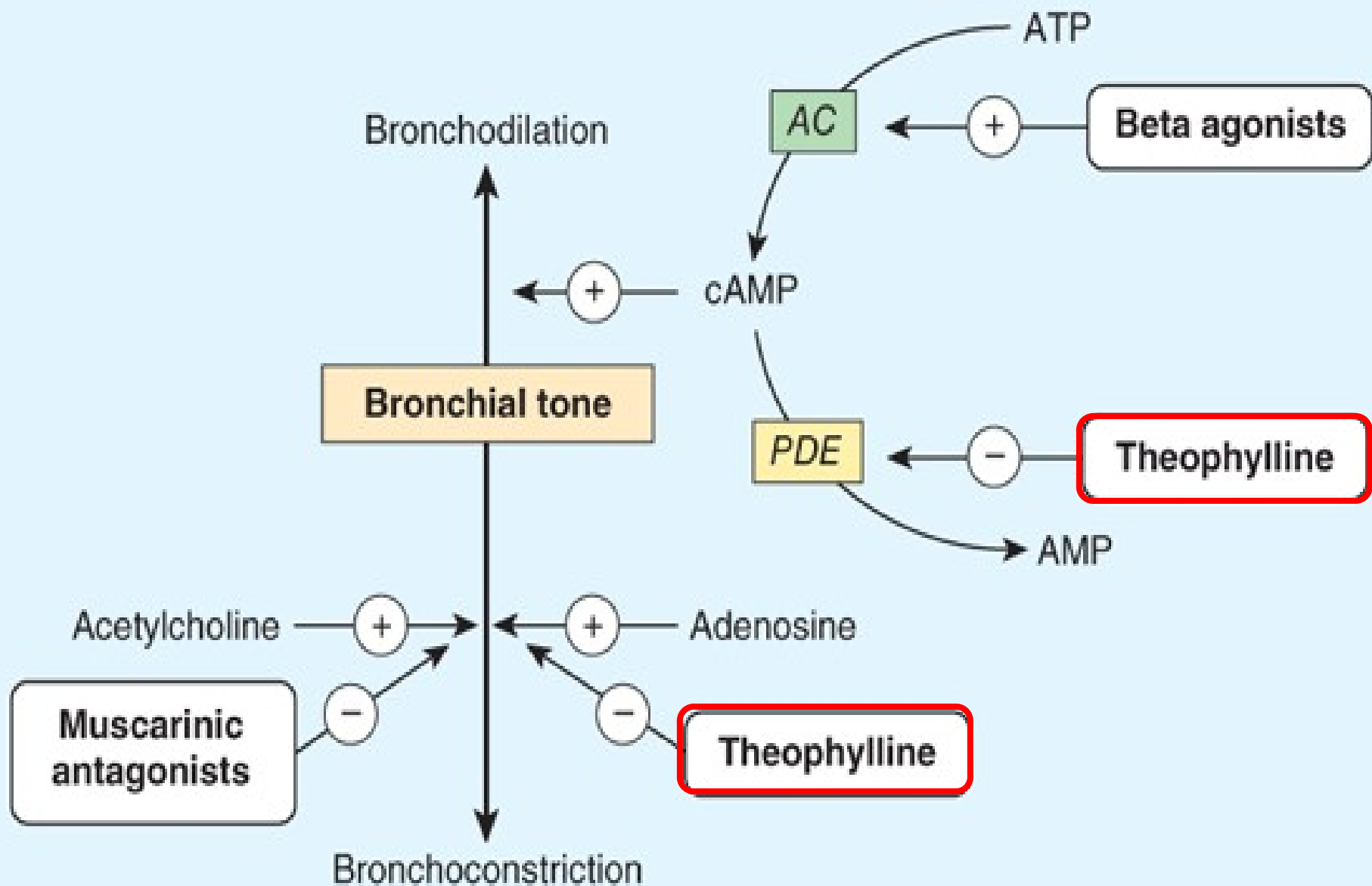
Muscarinic agonists

Bronchodilation

Bronchospasm

Adenosine





Sympathomimetics

Mechanism Of Action*

a) **Stimulate $\beta 2$ -receptors** $\rightarrow$ $\uparrow$ Adenylate cyclase enzyme

$\rightarrow \uparrow$ cAMP ----- Bronchodilatation

b) **Mast cell stabilization** $\rightarrow$ $\downarrow$ Release of Allergic mediators

c) $\square$ **Ciliary activity** $\square \square$ bronchial mucociliary transport



Sympathomimetics

:Members*

Non-Selective β -Agonists (β_1 , β_2 & α) -1

a- **Catecholamines:** Adrenaline &
.Isoprenaline

b- **Non-Catecholamines:** Ephedrine
Better avoided due to cardiac
side effects



Selective β_2 -agonists

Short Acting (SABA)
(Asthma relievers)

Salbutamol
Terbutaline

Used in
acute attack.

Long Acting (LABA)

“With corticosteroid”

Salmeterol
Formoterol

Used in prophylaxis

Bambuterol
(oral)



Salbutamol,
Terbutaline can be
.given orally



Adverse effects of β_2 agonists

- Tachycardia
- Tremors.
- Hypokalemia (due to $\square$ K entry into skeletal muscles) which may predispose to arrhythmias

β_2 adrenoceptor agonists are safe and effective bronchodilators when given in doses avoiding systemic adverse effects.

- If **LABA** used alone:

may increase the risk of asthma-related death
due to ischemia or arrhythmia

Therefore, they should be combined with inhaled corticosteroids

Which increase the sensitivity of B- receptors
which allow adding LABA in lower doses



Which of the following drugs is a bronchodilator that is used to relieve acute attack of bronchial asthma ?

- a)Salbutamol
- b)Budesonide
- c)Bambuterol
- d)Fluticasone
- e)Ciclesonide



Which of the following is a side effect of β 2-Agonists ?

- a)Bradycardia
- b)Hypokalemia
- c)Muscle Paralysis
- d)Dry cough
- e)Dysphonia



Methyl- xanthines

Mechanism of

1) Phosphodiesterase enzyme (PDE₃ & PDE₄):

result in accumulation of cellular c-AMP → **direct**

bronchodilatation.

The inhibition of PDE₄ in inflammatory cells:

the release of cytokines & cell migration.



Pharmacokinetics of Methyl-xanthines:

- Theophylline salts are used
- Sustained release tablets
are used to achieve serum levels for 12 h for:
 - less frequent administration, less fluctuation in serum levels,
more effective control for nocturnal asthma.
- Measuring blood levels : for patients on theophylline is important as it has a narrow therapeutic window.
- Therapeutic and toxic effects are related to plasma conc.
Therapeutic plasma conc . : 5-20 µg/L toxic level > 20 µg/L
- Theophylline is metabolized by liver :
inhibitors and inducers of liver enzymes !!!!
Interactions ???



Theophylline

a- Acute Attack of Asthma: Aminophylline 250 - 500 mg

SLOW ?? I.V injection

:Substitute Sympathomimetics when they are

□ Ineffective (Down-Regulation) □

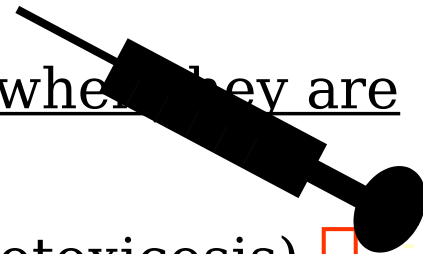
. □ or Contraindicated (Angina or Thyrotoxicosis) □

b- Severe Acute Attack = Status asthmaticus:

Aminophylline IV injection & Infusion as adjuvant to Hydrocortisone

c- Prophylaxis: **Oral Theophylline**

ORAL Slow Release (SR) tablets /12 hrs w

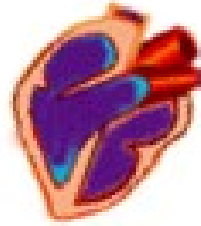




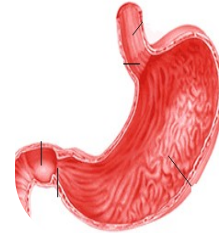
Adverse Effects of Methylxanthines



.C.N.S



.C.V.S



.G.I.T

Methylxanthines

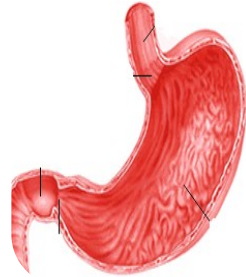


Adverse Effects of Theophylline

1- Narrow Safety Margine:

a- Therapeutic plasma level = 5 - 20 $\mu\text{g} / \text{ml}$

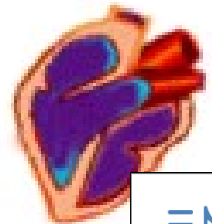
2- **G.I.T.** Orally $\rightarrow$ Anorexia, Nausea & Vomiting.
b- Toxic Plasma level $\rightarrow$ $> 20 \mu\text{g} / \text{ml}$



3- **C.N.S.** If Rectally !! Proctitis (irritant)
Headache, Nervousness,
Insomnia & **Convulsions**



4- **C.V.S.** : Tachycardia, Palpitation,
Arrhythmia But if : Rapid IV $\square$
Hypotension & Arrest



(velocity reaction)



Drug Interactions of

Theophylline is metabolized by liver :
Theophylline

i.e inhibitors and inducers of liver enzymes may lead to increase or decrease of plasma theophylline levels

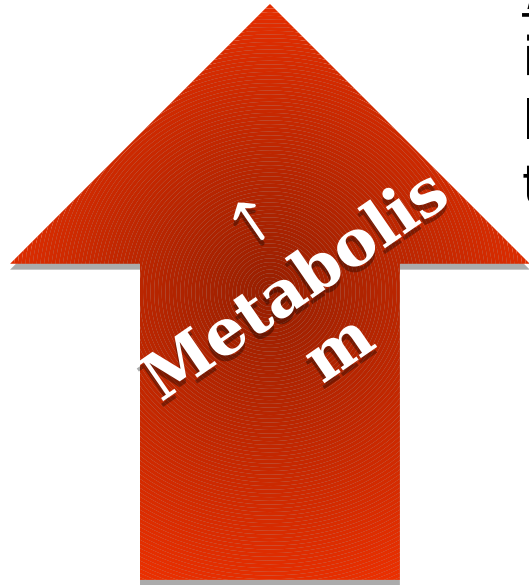
**Phenobarbitone, Phenytoin
& Carbamazepine.**

**[Hyperthyroidism Tobacco
& Alcohol.]**

Cimetidine

**Erythromycin &
Quinolones.**

**[Heart & Hepatic
Diseases and
Hypothyroidism]**



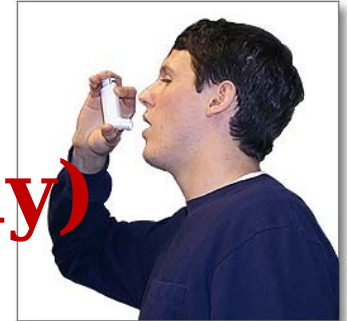
Which of the following drugs Block adenosine receptors and results in bronchodilatation ?

- a)Salbutamol
- b)Tiotropium
- c)Bambuterol
- d)Theophylline
- e)Ciclesonide



Anti- Muscarinic

Ipratropium bromide
Tiotropium bromide (once / day)



ADAM.

Mechanism of action:

- Block muscarinic receptors in the airways □
- prevent vagally mediated-bronchospasm
- decrease mucus gland hypersecretion



Anti-muscarinic drugs are used in:

1) Patients intolerant to inhaled β agonists

2) In addition to inhaled β agonists to add to their

bronchodilator

action in acute asthma exacerbations in emergency.

3) Patients of *chronic obstructive pulmonary disease*

Advantages of Ipratropium & Tiotropium over atropine

More selective in:

✓ bronchodilator action

✓ ↓ ↓ of mucous secretion in bronchial asthma

✓ Increase of the mucociliary clearance of secretion



Which of the following drugs is a bronchodilator that block muscarinic receptors and is taken once /day ?

- a) Salbutamol
- b) Tiotropium
- c) Bambuterol
- d) Theophylline
- e) Ipratropium

KEY Points Summary

❑ **B2 agonists :**

- Inhaled Short acting B2 agonists is used in acute attack
- Inhaled long acting B2 agonists is used in prophylaxis of asthma and must be combined with corticosteroids
- B2 agonists could result in tachycardia, tremors and hypokalemia

❑ **Methylxanthines**

- Bronchodilators with multiple mechanisms of actions
- Aminophylline must be given slowly IV to avoid [velocity reaction](#)
- Narrow safety margin
- Adverse effects: CNS stimulation ,gastric irritation and Arrhythmia

❑ **Antimuscarinics :**

- Ipratropium and tiotropium are bronchodilators that block muscarinic receptors

SUGGESTED TEXTBOOKS



1. Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7th edition.). Philadelphia: Wolters Kluwer
2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14th edition) New York: McGraw-Hill Medical.





Thank You

